

# Beneficial effects of postoperative radiotherapy for IIIA-N2 non-small cell lung cancer after radical resection analysed using the propensity score-matching method

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**Abstract.** The objective of the present study was to investigate the role of postoperative radiotherapy (PORT) after radical resection of stage IIIA-N2 non-small cell lung cancer (NSCLC). Subgroups of patients who benefited from PORT were evaluated. A retrospective review of 288 consecutive patients with resected pIIIA-N2 NSCLC at Beijing Chest Hospital (Beijing, China) was performed. Of these patients, 61 received PORT. The 288 patients were divided into PORT and non-PORT groups according to the treatment received. The baseline characteristics of the two patient groups were balanced using propensity score-matching (PSM; 1:1 matching). In total, 60 patients in the PORT group and 60 patients in the non-PORT group were matched. After PSM, the median survival time of the matched patients was 53 months. The 1-, 3- and 5-year overall survival (OS) rates of the PORT patient group were 95.0, 63.2 and 48.2%, respectively, while those of the non-PORT group were 86.7, 58.3 and 34.5%, respectively, and there was no significant difference between the two groups ( $P=0.056$ ). The 5-year local recurrence-free survival (LRFS) rate in the PORT group was significantly improved ( $P=0.001$ ). The effects of PORT on OS and LRFS rates were analysed in patients with different clinicopathological features. For subgroups with multiple N2

stations, N2 positive lymph nodes  $\geq 4$  and squamous cell carcinoma, PORT significantly increased the OS and LRFS rates ( $P<0.05$ ). In conclusion, there was no statistically significant improvement in the 5-year OS rate with PORT overall, but there may be subgroups, such as patients with multiple N2 stations, N2 positive nodes  $\geq 4$  and squamous cell carcinoma histology, that could be explored as potentially benefitting from improved 5-year OS and LRFS rates with PORT.

## Introduction

Stage III non-small cell lung cancer (NSCLC) accounts for one third of NSCLC at the time of initial diagnosis, and stage IIIA includes small tumors (T1a-T2b) with N2 involvement, large tumors (T3-T4) with N1 involvement and T4N0 [International Association for the Study of Lung Cancer (IASLC)/Union for International Cancer Control (UICC)/TNM staging system, 8th edition] (1). The survival of patients with stage IIIA NSCLC is poor: 55% of patients are alive at 24 months and the 5-year survival rate is 36% (2). Radiotherapy is an important treatment for which there are indications in all stages of lung cancer (3). For unresectable stage III NSCLC, thoracic radiotherapy with concurrent chemotherapy is the standard of care for the majority of patients (4). However, in patients with resected III-N+ NSCLC, postoperative radiotherapy (PORT) is not recommended in all patients. On one hand, PORT had a negative effect on the survival rate of patients with pN0 and pN1 disease (5). On the other hand, the effect of PORT on stage IIIA-N2 NSCLC has been controversial. There have been two large randomized clinical trial (RCT) studies (6,7) reporting the value of PORT for completely resected stage IIIA-N2 NSCLC. One is the LungART (6) study from Europe, which enrolled 501 patients (252 in the PORT group and 249 in the control group). The results confirmed that PORT reduced the mediastinal recurrence rate but did not significantly improve disease-free survival (DFS) rate (47 vs. 44%) or overall survival (OS) rate (67 vs. 69%). Another is the PORT-C study from China (7), which used modified intent-to-treat analysis and included 364 patients (184 in the PORT group and 180 in the observation group). There was no significant difference in

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*Abbreviations:* PORT, postoperative radiotherapy; NSCLC, non-small cell lung cancer; RCT, randomized clinical trial; DFS, disease-free survival; OS, overall survival; LRFS, local recurrence-free survival; DLNs, detected lymph nodes; PLNs, positive lymph nodes; POCT, postoperative adjuvant chemotherapy; CTV, clinical target volume; PSM, propensity score-matching

*Key words:* stage IIIA-N2 NSCLC, PORT, PSM

3-year OS (78.3 vs. 82.8%;  $P=0.93$ ), but PORT significantly improved the 3-year local recurrence-free survival (LRFS) rate (66.5 vs. 59.7%;  $P=0.03$ ). In addition, there was no significant difference in 3-year DFS (40.5 vs. 32.7%;  $P=0.20$ ). However, in a pre-planned yet exploratory analysis of the PORT-C study (7), DFS significantly differed after stratification according to the number of detected lymph nodes (DLNs) and positive lymph nodes (PLNs) [hazard ratio (HR), 0.75;  $P=0.04$ ].

As stage N2 NSCLC is a group of heterogeneous diseases, the efficacy of PORT may differ among subgroups with different clinicopathological features, such as the number of N2 stations (8,9), the number of N2 PLNs (10), histological type (11,12), smoking status (13), radiotherapy technology (14) and sex (15). Stage N2 NSCLC has a high risk of local recurrence (35-60%); therefore, some patients may still benefit from PORT (16,17). However, we hypothesised that not all patients may benefit from PORT. The present study aimed to screen the potential benefitting population of PORT through clinicopathological subgroup analysis.

## Materials and methods

**Patient selection.** Between October 2010 and September 2016, 288 consecutive patients with pathologically confirmed stage IIIA-N2 NSCLC (according to the 7th edition of IASLC/UICC/TNM) (2) were included in the study. Patients who survived >4 months after radical resection at the Beijing Chest Hospital (Beijing, China) were included. The main eligibility criteria were as follows: i) Eastern Cooperative Oncology Group performance status (PS) (18) of 0 or 1; ii) not having received neo-adjuvant chemotherapy or chemoradiotherapy; and iii) information about tumor characteristics, pathology and follow-up data being available. The mean age was 58 years (range, 31-80 years) and 63.2% of the included patients were male. The medical records and follow-up data of the patients were retrospectively analysed.

**Treatment.** The surgical methods for the 288 patients were divided into thoracic (261 cases) and thoracoscopic surgery (27 cases). Surgery included single lobectomy (212 cases), compound lobectomy (18 cases), sleeve resection (12 cases) and total lung resection (pneumonectomy; 46 cases). Surgical patients met the following criteria: i) PS of 0 or 1; ii) not having received neoadjuvant chemotherapy or chemoradiotherapy; iii) R0 radical surgical resection; and iv) complete mediastinal lymph node dissection or systematic mediastinal lymph node sampling performed during surgery.

Postoperative adjuvant chemotherapy (POCT) was administered with a cisplatin or carboplatin-based regimen (cisplatin, 75 mg/m<sup>2</sup>; carboplatin, area under the plasma drug concentration-time curve, 5), with a median of 4 cycles. A minority of patients did not receive POCT due to asthenia, refusal or the physician's decision (38 cases). PORT was performed on 61 patients. The administration of PORT was based on the radiation oncologist's decision or the surgeon's referral. Radiotherapy techniques included 3D conformal radiotherapy (21 cases) and intensity-modulated radiotherapy (40 cases). The clinical target volume (CTV) included subcarinal, ipsilateral paratracheal and ipsilateral hilar nodes, as well as involved nodes. The surgical margin of the stump

was also included in the CTV. The planning target volume was defined as the CTV plus 0.5-0.8-cm margins. The therapies were administered with a linear accelerator using a 6-8 MV X-ray at 180-200 cGy per fraction, 5 days per week, for a mean total radiation dose of 5,198 cGy. PORT was initiated at a mean of 4.38 months after surgery.

**Follow-up, evaluation of toxicity and survival.** Patients were regularly followed up every 3 months after surgery for the first 2 years and every 6-12 months thereafter. The last follow-up time was December 2019. Radiation pneumonitis and esophagitis were graded according to The Radiation Therapy Oncology Group criteria (19) and Common Terminology Criteria for Adverse Event version 4.0 (20), respectively. LRFS was defined from the day of surgery to the day of local recurrence (including surgical margin, ipsilateral hilar and/or mediastinum) or the last follow-up. OS was measured from the day of surgery to the date of death from any cause or to the last follow-up.

**Statistical analysis.** SPSS statistical software (version 26.0; IBM Corp.) was used for the statistical analyses. Data are presented as n (%). Due to the small number of positive cases (PORT group) and the large research time span in this retrospective case-controlled study, more data deviation and confounding variables could lead to unreliable results. Therefore, the regression data were analysed by the propensity score-matching (PSM) method, and patients with similar baseline data were matched to obtain the effect of the approximate RCT. Multiple logistic regression was used to calculate the propensity score of the PORT group (1:1 matching). Covariates included sex, age, smoking index [the pack-year index, which is calculated by multiplying the smoking period (years) by the number of packs of cigarettes smoked per day] (21), type of surgery, pathological tissue type, pathological T stage, number of N2 stations, number of N2 PLNs and POCT. Categorical variables were compared using the  $\chi^2$  test. The Kaplan-Meier method and the log-rank test were used for univariate analysis.  $P<0.05$  was considered to indicate a statistically significant difference.

## Results

**Patient characteristics.** A total of 288 analysable patients were included in the present study, of which 61 underwent PORT. Before PSM, there were 61 patients in the PORT group and 227 patients in the non-PORT group. There were statistically significant differences between the two groups for the type of surgery and POCT (performed vs. not performed), while there were no statistically significant differences for the other clinical factors. The clinical data of these patients were matched according to their PORT status with the PSM method (1:1 matching). A total of 60 patients were included in the PORT group and 60 patients were included in the non-PORT group after PSM. The general clinical data of the patients are shown in Table I. All factors were comparable after PSM matching ( $P>0.05$ ).

**Survival.** The median survival time of the 120 patients was 53 months. In Kaplan-Meier univariate analysis, the 1-, 3- and 5-year OS rates in the PORT group were 95.0, 63.2 and 48.2%, respectively, while the rates of the non-PORT group were 86.7, 58.3 and 34.5%, respectively ( $P=0.056$ ; Fig. 1A); however,

Table I. Patient characteristics.

Patient characteristic	Before PSM		P-value	After PSM		P-value
	Non-PORT, n (%) (n=227)	PORT, n (%) (n=61)		Non-PORT, n (%) (n=60)	PORT, n (%) (n=60)	
Sex			0.446			0.709
Female	81 (35.7)	25 (41.0)		23 (38.3)	25 (41.7)	
Male	146 (64.3)	36 (59.0)		37 (61.7)	35 (58.3)	
Age, years			0.128			0.827
<65	156 (68.7)	48 (78.7)		46 (76.7)	47 (78.3)	
≥65	71 (31.3)	13 (21.3)		14 (23.3)	13 (21.7)	
Smoking index, pack-year			0.072			0.705
<400	112 (49.3)	38 (62.3)		39 (65.0)	37 (61.7)	
≥400	115 (50.7)	23 (37.7)		21 (35.0)	23 (38.3)	
Type of surgery			0.024			>0.999
Lobectomy	185 (81.5)	57 (93.4)		56 (93.3)	56 (93.3)	
Pneumonectomy	42 (18.5)	4 (6.6)		4 (6.7)	4 (6.7)	
Histology			0.753			0.540
SCC	66 (29.1)	19 (31.1)		15 (25.0)	18 (30.0)	
Non-SCC	161 (70.9)	42 (68.9)		45 (75.0)	42 (70.0)	
Pathological T stage			0.544			0.274
T1-2	178 (78.4)	50 (82.0)		44 (73.3)	49 (81.7)	
T3	49 (21.6)	11 (18.0)		16 (26.7)	11 (18.3)	
No. of N2 stations			0.622			0.261
Single	63 (27.8)	15 (24.6)		10 (16.7)	15 (25.0)	
Multiple	164 (72.2)	46 (75.4)		50 (83.3)	45 (75.0)	
No. of N2 positive nodes			0.135			0.850
1-3	110 (48.5)	23 (37.7)		22 (36.7)	23 (38.3)	
≥4	117 (51.5)	38 (62.3)		38 (63.3)	37 (61.7)	
POCT			0.031			0.309
No	35 (15.4)	3 (4.9)		1 (1.7)	3 (5.0)	
Yes	192 (84.6)	58 (95.1)		59 (98.3)	57 (95.0)	

PSM, propensity score-matching; SCC, squamous cell carcinoma; PORT, postoperative radiotherapy; POCT, postoperative chemotherapy.

there was no significant difference between the two groups. The 1-, 3- and 5-year LRFS rates in the PORT group were 95.0, 65.0 and 47.5%, respectively, while the rates of the non-PORT group were 68.3, 41.7 and 27.3%, respectively (P=0.001; Fig. 1B).

The Kaplan-Meier method was also used to analyse the effect of PORT on OS and LRFS in patients in different subgroups based on clinicopathological features. In the subgroups of number of N2 stations (multiple stations; P=0.035; Fig. 2A), number of N2 PLNs (≥4; P=0.019; Fig. 2B), histology (squamous cell carcinoma; P=0.006; Fig. 2C) and type of surgery (pneumonectomy, P=0.017; Fig. 2G), the 5-year OS time of the PORT group was significantly prolonged compared with that of the non-PORT group. In the additional clinicopathological subgroups, there was no significant difference between the two groups in terms of sex, age, smoking index, type of surgery (lobectomy), histology (non-squamous cell carcinoma), T stage, number of N2 stations (single station), number of N2 PLNs (1-3) or POCT in terms of the 5-year OS rate (Table II).

Compared with that in the non-PORT group, the 5-year LRFS rate in the PORT group was significantly different in several clinicopathological subgroups. Notably, in the PORT group, the 5-year LRFS rate was improved in three subgroups: Number of N2 stations (multiple stations; P=0.002; Fig. 2D), number of N2 PLNs (≥4; P=0.001; Fig. 2E) and histology (squamous cell carcinoma; P<0.001; Fig. 2F). There were also statistically significant differences observed in terms of sex, age (<65 years), smoking index, type of surgery (lobectomy), pT stage (T1-2) and POCT (yes) (Table II). Therefore, for subgroups of patients with multiple N2 stations, N2 positive lymph nodes ≥4 and squamous cell carcinoma, PORT significantly increased the OS and LRFS rates (Table II).

## Discussion

A meta-analysis published in 1998 (5) demonstrated that PORT had an adverse effect on patients with NSCLC after

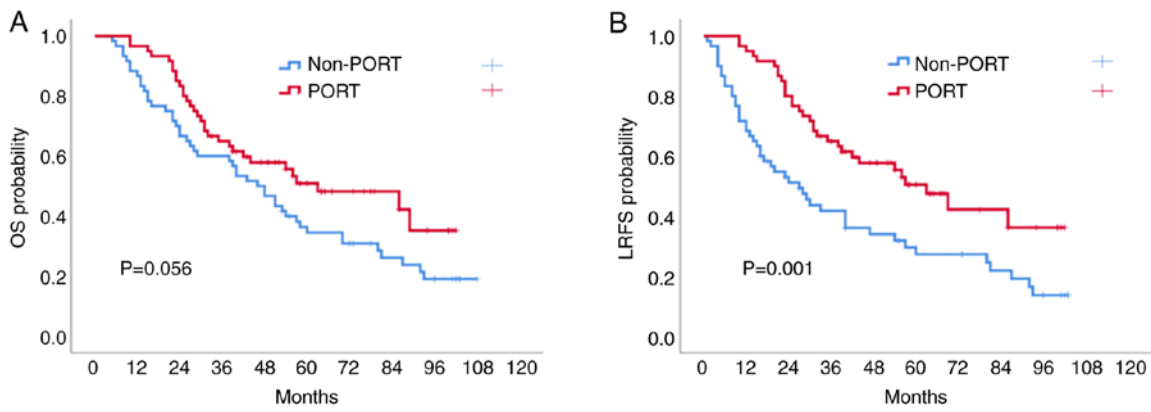


Figure 1. OS and LRFS of patients according to PORT after PSM. (A) OS curves after PSM. The 5-year OS rate was 48.2% for the PORT group and 34.5% for the non-PORT group. The median OS time was 63 months (95% CI, 30.56-95.44) for the PORT group and 45 months (95% CI, 34.61-57.39) for the non-PORT group. (B) LRFS curves after PSM. The 5-year LRFS rate was 47.5% for the PORT group and 27.3% for the non-PORT group. The median LRFS time was 63 months (95% CI, 47.19-78.82) for the PORT group and 27 months (95% CI, 16.06-37.94) for the non-PORT group. LRFS, local recurrence-free survival; OS, overall survival; PORT, postoperative radiotherapy; PSM, propensity score-matching.

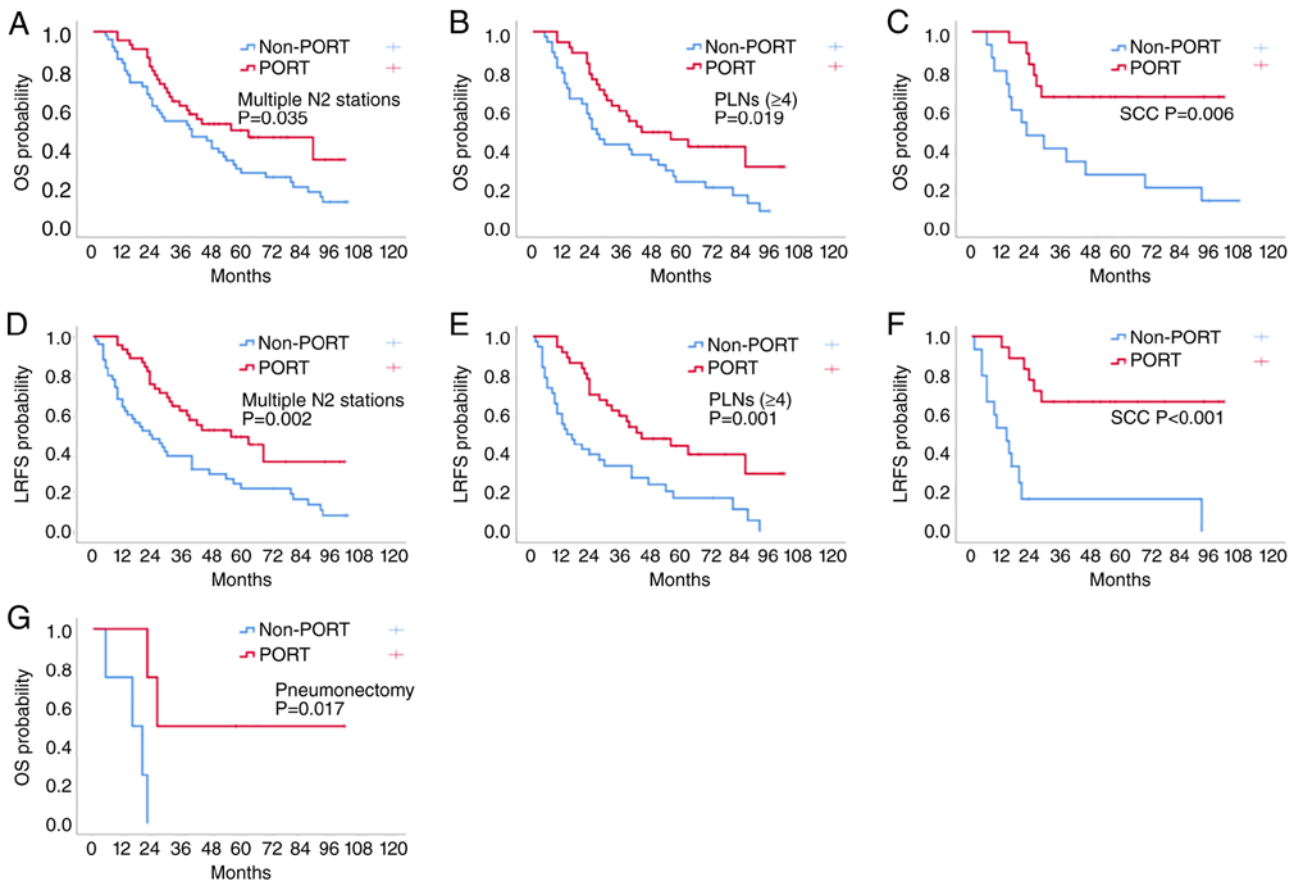


Figure 2. OS and LRFS of patients in different clinicopathological subgroups according to the use of PORT after propensity score-matching. (A) OS curves for patients with multiple N2 stations. The 5-year OS rate was 49.3% for the PORT group and 27.5% for the non-PORT group. (B) OS curves for patients with N2 PLNs ( $\geq 4$ ). The 5-year OS rate was 44.6% for the PORT group and 23.0% for the non-PORT group. (C) OS curves for patients with SCC. The 5-year OS rate was 66.7% for the PORT group and 26.7% for the non-PORT group. (D) LRFS curves for patients with multiple N2 stations. The 5-year LRFS rate was 48.7% for the PORT group and 22.0% for the non-PORT group. (E) LRFS curves for patients with N2 PLNs ( $\geq 4$ ). The 5-year LRFS rate was 43.8% for the PORT group and 17.2% for the non-PORT group. (F) LRFS curves for patients with SCC. The 5-year LRFS rate was 66.7% for the PORT group and 16.7% for the non-PORT group. (G) OS curves for patients with pneumonectomy. The 5-year OS rate was 50.0% for the PORT group and 0% for the non-PORT group. LRFS, local recurrence-free survival; OS, overall survival; PLNs, positive lymph nodes; PORT, postoperative radiotherapy; SCC, squamous cell carcinoma.

complete resection (HR, 1.21; 95% CI, 1.08-1.34). Subgroup analysis demonstrated that for patients with N0-N1 NSCLC, there was no significant improvement in survival rate,

which was related to the then available 2D radiotherapy technology (22). However, for patients with N2 NSCLC, the value of PORT was not clear. With the improvements

Table II. OS and LRFS rates of patients with different clinicopathological features according to the use of PORT after propensity score-matching.

Clinicopathological feature	5-year OS rate			5-year LRFS rate		
	Non-PORT, %	PORT, %	P-value	Non-PORT, %	PORT, %	P-value
Sex						
Female	33.5	59.5	0.203	27.2	58.7	0.037
Male	34.9	45.9	0.137	27.2	45.9	0.008
Age, years						
<65	34.5	48.5	0.198	25.0	47.8	0.008
≥65	33.3	59.3	0.131	34.3	59.3	0.064
Smoking index, pack-year						
<400	40.3	57.1	0.166	33.3	56.4	0.028
≥400	23.8	41.2	0.121	15.4	41.2	0.005
Type of surgery						
Lobectomy	36.9	50.7	0.149	29.3	50.2	0.006
Pneumonectomy	0.0	50.0	0.017	0.0	50.0	0.051
Histology						
SCC	26.7	66.7	0.006	16.7	66.7	<0.001
Non-SCC	36.9	45.6	0.560	31.9	44.8	0.170
Pathological T stage						
T1-2	35.5	51.5	0.173	29.2	50.8	0.012
T3	31.3	45.5	0.179	21.9	45.5	0.050
No. of N2 stations						
Single	70.0	55.9	0.613	58.3	55.9	0.823
Multiple	27.5	49.3	0.035	22.0	48.7	0.002
No. of N2 positive nodes						
1-3	54.2	61.0	0.778	44.7	61.0	0.213
≥4	23.0	44.6	0.019	17.2	43.8	0.001
POCT						
No	0.0	66.7	0.083	0.0	66.7	0.083
Yes	35.1	50.2	0.077	27.7	49.7	0.002

Kaplan-Meier analysis followed by log-rank test for various subgroups. P-values were calculated by comparing the PORT and non-PORT groups. OS, overall survival; LRFS, local recurrence free survival; SCC, squamous cell carcinoma; PORT, postoperative radiotherapy; POCT, postoperative chemotherapy.

of radiotherapy technology, the damage to normal tissues caused by radiotherapy has decreased. Therefore, the role of PORT in patients with resected N2 NSCLC should be re-evaluated. In 2006, a retrospective analysis of 7,465 postoperative patients with stage II-III NSCLC based on the Surveillance, Epidemiology and End Results (SEER) database demonstrated that although PORT reduced the survival rate of patients with N0-1 NSCLC, it also improved the survival rate of patients with N2 NSCLC (HR, 0.855; P=0.008) (23). Similarly, in 2015, a retrospective analysis of patients with stage pN2 NSCLC after radical operation (stratified based on the use of PORT) based on the National Cancer Database demonstrated that the 5-year median OS time in the PORT group was significantly increased compared with that in the non-PORT group (45.2 and 40.7 months, respectively), and the 5-year OS rate was 34.7% in the non-PORT group, while that

in the PORT group was 39.8% in (P=0.014) (24). In 2018, an updated meta-analysis also demonstrated that PORT increased the 5-year OS rate by 8% (P=0.008) in patients with resectable stage IIIA-N2 NSCLC, with significantly increased DFS rate (HR, 0.70; P<0.0001) and LRFS rate (HR, 0.37; P<0.0001) (25). Based on the aforementioned conclusions, the value of PORT after radical resection of stage IIIA-N2 NSCLC remains controversial and there is still a lack of high-level evidence.

Recently, two large RCT studies (6,7) evaluated the efficacy of PORT in stage IIIA-N2 NSCLC with complete resection. The European LungART (6) study was the first randomised phase 3 study evaluating the role of 3D-conformal PORT after a considered complete resection of stage IIIA-N2 NSCLC, which demonstrated no decrease in the risk of death or disease progression for PORT. The 3-year OS rate was 69% in the control group and 67% in the PORT group. In the present

study, the 5-year OS rates of the PORT group and non-PORT group after PSM were 48.2 and 34.5%, respectively. PORT tended to increase the OS rate, but it did not achieve statistical significance ( $P=0.056$ ). In the present study, lymph node status subgroups, such as multiple lymph node stations and  $\geq 4$  nodes subgroups, were important subgroups of patients who benefited from PORT, which was not explored in the LungART study. One interesting aspect is that, compared with the LungART study, the ratio of multiple N2 stations in the present study was higher. The lymph node metastasis subgroups (multiple N2 stations and N2 positive lymph nodes  $\geq 4$ ) may be important subgroups of patients who may benefit from PORT. The present study also demonstrated a significant improvement in LRFS rate by PORT (5-year LRFS, 47.5 vs. 27.3%;  $P=0.001$ ). The same conclusion was reached in another large RCT study (7), with the number of DLNs and PLNs supporting the hypothesis that the PORT group had an improved prognosis ( $P=0.04$ ) after stratified analysis. It reached a conclusion that the cohort with a higher number of PLNs may benefit from PORT. Since N2 stage NSCLC is a group of heterogeneous diseases, and not all patients may benefit from PORT, further research is required to precisely identify the population that may benefit from PORT based on more detailed clinical characteristics.

The efficacy of PORT after radical surgery in patients with stage IIIA-N2 NSCLC is affected by numerous clinical factors. Among these, mediastinal PLN status is the most studied. Riquet *et al* (26) compared patients with multiple station N2 metastasis and single station N2 metastasis in N2 stage NSCLC after complete resection who had 5-year OS rates of 28.5 and 17.2%, respectively ( $P=0.0002$ ). The purpose of PORT is to reduce the recurrence rate in the mediastinum, and it may reduce distant metastasis. Matsuguma *et al* (8) retrospectively analysed stage IIIA-N2 NSCLC after complete resection. The results demonstrated that in patients with multiple station metastasis N2, the DFS rate in the PORT group (41.7%) was significantly higher than that of the non-PORT group (5.9%;  $P=0.02$ ). Another retrospective study of patients with multiple station pN2 NSCLC also concluded that the local control rate (66.0 vs. 29.4%;  $P=0.011$ ) and DFS rate (43.2 vs. 16.6%;  $P=0.037$ ) were significantly improved in the PORT group in contrast to the non-PORT group (9). Wang *et al* (10) analysed 3,377 patients with stage IIIA-N2 NSCLC in the SEER database and demonstrated that the use of PORT significantly improved OS rate (HR, 0.803; 95% CI, 0.687-0.938;  $P=0.006$ ) and lung cancer-specific survival rate (HR, 0.794; 95% CI, 0.671-0.94;  $P=0.007$ ) in the positive lymph nodes ( $n>3$ ) subgroup, while the use of PORT was not associated with an advantage in the positive lymph nodes ( $n\leq 3$ ) subgroup. The efficacy of PORT in patients with different pathological types after radical resection of stage IIIA-N2 NSCLC is also different. In patients with resectable N2 NSCLC, squamous cell carcinoma has a higher local failure rate (21 vs. 14%) and a lower distant failure rate (7 vs. 11%) compared with adenocarcinoma (25). Therefore, the use of PORT to eradicate minimal residual disease may reduce the risk of tumour metastasis in the mediastinum (27). Hui *et al* (11) retrospectively analysed 221 patients with stage IIIA-N2 NSCLC after resection and demonstrated that PORT increased the 5-year OS rate, and the subgroup analysis demonstrated that PORT significantly

improved the OS of groups with squamous cell carcinoma ( $P=0.013$ ) and N2 PLNs  $\geq 4$  ( $P=0.025$ ). Therefore, the contribution of PORT was different in different histological types of stage IIIA-N2 NSCLC after resection, and PORT may be more beneficial in patients with squamous cell carcinoma. The present study found that PORT was beneficial in the multiple station N2, N2 PLNs  $\geq 4$  and squamous cell carcinoma subgroups.

However, there were some limitations of the present study. Firstly, this was a retrospective study with small subgroup analyses and the findings are exploratory rather than definite, and the number of patients who received PORT was small. Resected pIIIA-N2 NSCLC is a heterogeneous group of diseases, and not all patients benefited from PORT in the present study. However, it is interesting to note that the LungART trial did not explore the clinical subgroups benefiting from PORT in detail (6). Secondly, after PSM, there was a smaller proportion of patients treated with pneumonectomy or POCT in the subgroup, which may have reduced the statistical efficiency of the conclusions made. Thirdly, the present study was retrospective and with the shortcoming that pathologists did not report the extranodal extension (ENE) of nodal metastases. ENE is an important prognostic factor in NSCLC (28). It is suggested that ENE should be added as an important subgroup factor for future RCT studies to evaluate the role of PORT in IIIA-N2 NSCLC after radical resection.

In conclusion, PORT is not a novel clinical process after NSCLC resection; however, the role of PORT in patients with stage III-N2 NSCLC has remained controversial for a long time. Some results from the LungART trial are unpublished and explorative analysis from this trial will be reported in detail in the future (6). The present study indicated that there may be some patients who may benefit from PORT. In total, 82% of European radiation oncology experts still use PORT for patients with stage III pN2 NSCLC with risk factors, such as multi-station/-level lymph nodes (29). The present study demonstrated that there may be some subgroups of patients after resection of pIIIA-N2 NSCLC, such as multiple station N2, N2 PLNs  $\geq 4$  and squamous cell carcinoma subgroups, which may benefit from PORT.

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### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Authors' contributions

CT conceived the idea for the study. BL took part in all planning. CT, GL, YX, GX, TZ, JH, FL and BL designed the study, collected the data, analyzed the data, and drafted the article. CT and FL assisted in the application of statistical methods. CT and BL confirm the authenticity of all the raw data. All authors critically revised the manuscript. All authors have read and approved the final manuscript.

## Ethics approval and consent to participate

The Ethics Committee of The Academic Research Project at the Beijing Tuberculosis and Thoracic Tumor Research Institute/Beijing Chest Hospital (Beijing, China; ethical approval no. 2019-47) approved the present study. Written informed consent was obtained from all participants.

## Patient consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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